TSC1 gene

tuberous sclerosis 1

Normal Function

The *TSC1* gene provides instructions for producing a protein called hamartin, whose function is not fully understood. Within cells, hamartin interacts with a protein called tuberin, which is produced from the *TSC2* gene. These two proteins help control cell growth and size. Proteins that normally prevent cells from growing and dividing too fast or in an uncontrolled way are known as tumor suppressors. Hamartin and tuberin carry out their tumor suppressor function by interacting with and regulating a wide variety of other proteins.

Health Conditions Related to Genetic Changes

bladder cancer

Somatic mutations of the *TSC1* gene that occur in bladder cells are associated with some cases of bladder cancer. In some of these cells, one copy of the *TSC1* gene is missing because the region of chromosome 9 containing the gene has been deleted; the other copy of the gene has a mutation that interferes with its function. As a result, little or no hamartin is produced. A loss of hamartin in bladder cells may allow these cells to grow and divide without control, leading to the formation of a cancerous tumor.

It is unclear why inherited *TSC1* gene mutations lead to the noncancerous growths characteristic of tuberous sclerosis complex, while somatic mutations in this gene are associated with the development of cancerous tumors.

lymphangioleiomyomatosis

Mutations in the *TSC1* gene can cause a disorder called lymphangioleiomyomatosis (LAM), although mutations in the *TSC2* gene appear to be responsible for most cases of this disorder. This destructive lung disease is caused by the abnormal overgrowth of smooth muscle-like tissue in the lungs. It occurs almost exclusively in women, causing coughing, shortness of breath, chest pain, and lung collapse.

LAM can occur alone (isolated or sporadic LAM) or in combination with a condition called tuberous sclerosis complex (described below). Researchers suggest that sporadic LAM can be caused by a random mutation in the *TSC1* gene that occurs very early in development. As a result, some of the body's cells have a normal version of the gene, while others have the mutated version. This situation is called

mosaicism. When a mutation occurs in the other copy of the *TSC1* gene in certain cells during a woman's lifetime (a somatic mutation), she may develop LAM.

tuberous sclerosis complex

More than 400 mutations in the *TSC1* gene have been identified in individuals with tuberous sclerosis complex, a condition characterized by developmental problems and the growth of noncancerous tumors in many parts of the body. Most of these mutations involve either small deletions or insertions of DNA in the *TSC1* gene. Some mutations create a premature stop signal in the instructions for making hamartin.

People with *TSC1*-related tuberous sclerosis complex are born with one mutated copy of the *TSC1* gene in each cell. This mutation prevents the cell from making functional hamartin from that copy of the gene. However, enough hamartin is usually produced from the other, normal copy of the *TSC1* gene to regulate cell growth effectively. For some types of tumors to develop, a second mutation involving the other copy of the gene must occur in certain cells during a person's lifetime.

When both copies of the *TSC1* gene are mutated in a particular cell, that cell cannot produce any functional hamartin. The loss of this protein allows the cell to grow and divide in an uncontrolled way to form a tumor. A shortage of hamartin also interferes with the normal development of certain cells. In people with *TSC1*-related tuberous sclerosis complex, a second *TSC1* gene mutation typically occurs in multiple cells over an affected person's lifetime. The loss of hamartin in different types of cells disrupts normal development and leads to the growth of tumors in many different organs and tissues.

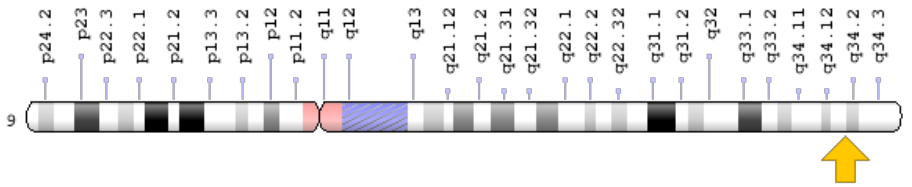
other disorders

Inherited mutations in the *TSC1* gene can cause a disorder known as focal cortical dysplasia of Taylor balloon cell type. This disorder involves malformations of the cerebrum, the large, frontal part of the brain that is responsible for thinking and learning. Focal cortical dysplasia causes severe recurrent seizures (epilepsy) in affected individuals.

Chromosomal Location

Cytogenetic Location: 9q34.13, which is the long (q) arm of chromosome 9 at position 34.13

Molecular Location: base pairs 132,891,348 to 132,945,269 on chromosome 9 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- hamartin
- KIAA0243
- TSC1_HUMAN

Additional Information & Resources

Educational Resources

- Cancer Medicine (sixth edition, 2003): Tuberous Sclerosis
  https://www.ncbi.nlm.nih.gov/books/NBK13658/#A19617

GeneReviews

- Tuberous Sclerosis Complex
  https://www.ncbi.nlm.nih.gov/books/NBK1220

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28TSC1%5BTIAB%5D%29+OR+%28hamartin%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

OMIM

- FOCAL CORTICAL DYSPLASIA OF TAYLOR
  http://omim.org/entry/607341
- TSC1 GENE
  http://omim.org/entry/605284

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/TSC1ID183.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=TSC1%5Bgene%5D
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=12362
- Leiden Open Variation Database: TSC1 Homepage
  http://chromium.lovd.nl/LOVD2/TSC/home.php?select_db=TSC1
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/7248
- UniProt
  http://www.uniprot.org/uniprot/Q92574

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